

REMARKS

The Claims were 1-5. Claims 1 and 11 have been amended, Claims 2, 4-6, 8-10, 12, 14, 16, 18, 20-26 and 28-31 have been canceled and claim 33 has been added. Thus, Claims 1, 3, 7, 11, 13, 15, 17, 19, 27, 32 and 33 are pending in this case all to more clearly and distinctly claim Applicant's invention. New Claim 33 introduces no new matter and is fully supported by the specification. Applicant respectfully request entry of the amendments as they place the application in condition for allowance or in better condition for possible appeal.

Claim 1 has been amended to fix a typographical error by the delete phrase “, a phosphoric acid group, or a carboxylic acid group”. Claim 11 has been amended to depend on claim 3. New Claim 33 depends appropriately from Claim 32 and introduces no new matter. Note that new Claim 33 is the same as canceled Claim 9. Accordingly, it is respectfully submitted that no new matter has been added by the amendments.

Claim Objections

The Examiner objects to claim 9 because claims should depend on preceding claims. To expedite prosecution of the application, Applicants have canceled claim 9 and add new claim 23 which is identical to claim 9.

Rejection Based On 35 U.S.C. 112, Second Paragraph

The Examiner rejects Claim 11 as being infinite under 35 U.S. C. §112, second paragraph, for failing to particularly point out and distinctly claim the subject matter which applicants regards as the invention. More particularly, the Examiner rejects claim 11 because it is unclear as to which claim it depends on.

In order to expedite prosecution, Applicants have amended claim 11 to depend on claim 3. Therefore, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Rejection Based On Brush In View Of Haugland Under 35 U.S.C. § 103 (a)

The Examiner rejects Claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 27 and 31 under 35 U.S.C. § 103 (a) as being unpatentable over U.S. Patent No. 5,986,086 to Brush et al. ("Brush") in view of U.S. Patent No. 5,719,031 to Haugland et al. ("Haugland"). Applicants respectfully traverse this rejection.

The Examiner concedes that Brush does not teach have a water soluble group other than a sulfonic acid group, phosphoric acid or carboxylic group. The Examiner then refers to Haugland for teaching using sulfonamide in the dye to attach to nucleotide. The Examiner asserts that one of ordinary skill in the art at the time the invention was made would have been motivated to incorporate the teaching of sulfonamide in Haugland into the fluorescent dye of Brush in order to attach the dye to the nucleotide. Also, the Examiner asserts that Haugland states that sulfonamide or amine successfully bound the oligonucleotide to the fluorophore. Thus, the Examiner concludes that it would have been prima facie obvious to apply the successfully use of

sulfonamide of Haugland to attach dyes to oligonucleotides in order to successfully attach fluorescent dyes to Brush's nucleotide. Applicants respectfully disagree.

To establish obviousness of a claimed invention, all claim elements must be disclosed, taught or suggested by the prior art. As stated above, independent Claim 1 has been currently amended. Claim 1 has been currently amended to claim a fluorescent nucleotide represented by the formula: A-B-C, wherein A represents a residue of natural or synthetic nucleotide, oligonucleotide, polynucleotide, or derivative thereof, and binds to B at a base moiety in said residue; B represents a divalent linking group or a single bond; and C represents a monovalent group derived from a fluorescent dye having no sulfonic acid group and no phosphoric acid group in a molecule, and having sulfonamide group or a lower alcohol group in said molecule.

Brush teaches a non-sulfonated cyanine dyes for labeling nucleosides and nucleotides. See column 2, lines 32-34. However, Applicants agree with the Examiner that Brush does not teach having a water soluble group other than a sulfonic acid group, phosphoric acid or carboxylic group. Brush also does not teach a fluorescent dye having sulfonamide group or a lower alcohol group.

In regards to Haugland, Haugland discloses dye labeled polymers as reagents for measuring polymer degradation. Haugland teaches using a sulfonamide in the dye as a spacer or linker to attach the functional group on the polymer and the reactive group on the fluorophore, where the polymer may be a nucleotide. See column 7, lines 28-37. This is unlike the present invention in which a water-soluble functional group, such as sulfonamide and lower alcohol, is introduced into the fluorescent dye. See paragraph [0041]. The purpose of the addition of the water-soluble functional group is to prevent fluorescent dyes of high molecular weights from becoming insoluble due to reduction of functional groups having negative charges. See paragraph [0041]. In other words, the water-soluble function group aid in the solubility of the

dye and the fluorescent intensity of the dye. Further, this is demonstrated in the Examples of the present application. The fluorescent intensities of Compounds 5-8 are stronger than the comparative dye Cy-5-dUTP (from Amersham) or Cy-3-dUTP (from Amersham), as shown in Tables 1 and 2 on pages 27 and 28 of the present application. Cy-5-dUTP and Cy-3-dUTP are dyes having a sulfonic acid (salt), but not having a sulfonamide group or a lower alcohol group, as presently claimed. The advantage of the present invention is achieved by using a dye having no sulfonic acid group and no phosphoric acid and having a sulfonamide or a lower alcohol.

Accordingly, Brush does not teach a fluorescent dye having sulfonamide group or a lower alcohol group. Also, Haugland does not teach the property of the sulfonamide as a water-soluble group. Thus, the Applicants believe that the present invention is not obvious over the teaching of Brush in view of Haugland since Brush and/or Haugland does not teach, disclose or suggest the present claims. Moreover, one skilled in the art would find nothing in Brush or Haugland alone or in combination that would disclose, teach or suggest the claimed invention or any reason for making it. Further, there is no motivation to combine the references in such a way to get the claimed invention. Therefore, an obvious rejection under 35 U.S.C. §103 (a) is improper.

Rejection Based On Brush In View Of Haugland In Further View Of Mao Under 35 U.S.C.

§ 103 (a)

The Examiner rejects Claims 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 27 and 31 under 35 U.S.C. § 103 (a) as being unpatentable over U.S. Patent No. 5,986,086 to Brush et al. ("Brush") in view of U.S. Patent No. 5,719,031 to Haugland et al. ("Haugland") in further view of U.S. Patent No. 6,130,101 to Mao et al. ("Mao"). Applicants respectfully traverse this rejection.

The Examiner concedes that Brush does not teach an aminoallyl linkage. The Examiner then refers to Mao for teaching aminoallyl linkage in binding dyes to nucleotides. The Examiner asserts that one of ordinary skill in the art at the time the invention was made would have been motivated to apply the aminoallyl linkage of Mao to Brush's dye in order to provide a stable bond. Thus, the Examiner concludes that it would have been prima facie obvious to apply the aminoallyl linkage to Brush's dye in order to create a strong link to the nucleotide. Applicants respectfully disagree.

To establish obviousness of a claimed invention, all claim elements must be disclosed, taught or suggested by the prior art. As stated above, independent Claim 1 has been currently amended. Brush does not teach a fluorescent dye having sulfonamide group or a lower alcohol group or an aminoallyl linkage. Also, Haugland does not teach the property of the sulfonamide as a water-soluble group.

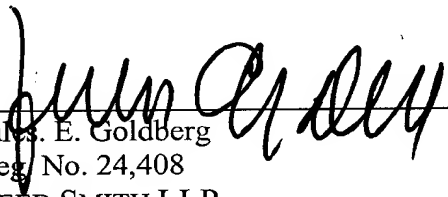
Mao teaches sulfonated xanthene derivative that are useful as fluorescent probes. See Abstract. However, Mao does not cure the deficiencies of the cited prior art. Thus, the Applicants believe that the present invention is not obvious over the teaching of Brush in view of Haugland and further in view of Mao since Brush, Haugland and/or Mao does not teach, disclose or suggest the present claims. Moreover, one skilled in the art would find nothing in Brush, Haugland or Mao alone or in combination that would disclose, teach or suggest the claimed invention or any reason for making it. Further, there is no motivation to combine the references in such a way to get the claimed invention. Therefore, an obvious rejection under 35 U.S.C. §103 (a) is improper.

In view of the remarks presented herein, it is respectfully submitted that the present application is in condition for final allowance and notice to such effect is requested. If the Examiner believes that additional issues need to be resolved before this application can be passed to issue, the undersigned invites the Examiner to contact him at the telephone number provided below.

Respectfully submitted,

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By



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